The IAS statin literature update will keep you up-to-date with all recent statin publications, using a curated approach to select relevant articles.

Key publications

Premature atherosclerosis insufficiently recognized and managed

Premature atherosclerosis (PAS) is diagnosed if individuals have manifestations of CAD before the age of 50 in males and females before 55 years. Strategies to prevent PAS are underserved in current updated guidelines. Based on data collected in the Study to Avoid CardioVascular Events in British Columbia (SAVE BC), PAS patients were evaluated. CAD was defined as angiographically-confirmed CAD with stenosis of >50% in at least one coronary artery in patients presenting with the first STEMI, NSTEMI, unstable or stable angina, or referred electively for angiography. Included in the analysis were 417 patients (28.1% females). Almost all patients (94.3%) were found to have at least one of six major
CVRFs: dyslipidemia (68.6%, including 14.1% of patients with LDL-C ≥5 mmol/L), hypertension (47.0%), family history of premature CVD (40.8%), obesity (40.6%), current smoking (26.9%), or diabetes (26.9%). Based on guideline recommendations from the American College of Cardiology/American Heart Association, Canadian Cardiovascular Society, and European Society of Cardiology guidelines, 47.7%, 61.4%, and 34.3%, respectively, were eligible for statin therapy. Statins were used by 17.1%, and only 11.0% achieved guideline-recommended LDL-c targets. Increased plasma lipids and diabetes showed a positive association with statin use; smoking was associated with non-treatment. These findings warrant new effective strategies and guidelines to improve screening and management strategies for premature CAD.


PCSK9ab associated with renal side effects

In the recently updated ACC/AHA lipid management guidelines, the addition of PCSK9ab has been recommended (Class IIa) for high-risk patients that show insufficient LDL-c lowering response to maximally tolerated high dose high, intensity statin plus ezetimibe. In the major trials that evaluated the efficacy and safety of PCSK9ab therapy, this class of drugs has shown an excellent safety profile. In this case report, a patient with advanced renal disease and statin intolerance developed an acute tubular injury, confirmed with renal biopsy after PCSK9ab were initiated. Stopping the therapy resulted in creatinine clearance returning to baseline levels. This rare side effect was reported in only two other case reports, one patient with advanced renal disease and a patient with normal renal function. The potential mechanism causing renal harm remains elusive; potentially, emollients of the injectable drug could be responsible for the renal effects. PCSK9ab are considered as a very safe injectable class of drugs; however, with increasing numbers of patients using PCSK9ab real world data will expand, as will the number of novel side effects undetected in the clinical trials due to the rarity of certain adverse events as the one reported in this case report. Being aware of these uncommon adverse occurrences early, can prevent the progression of serious complications.


IVUS progression in patients with absent modifiable risk factors

Do patients in whom common modifiable risk factors are absent show signs of coronary
artery atherosclerosis (AS) and progression of AS. An intriguing question was explored by comparing participants (N=5823) in ten clinical trials that evaluated IVUS imaging to determine the effects of medical therapies on plaque progression. A total of 165 (2.8%) patients were found to have no self-reported common modifiable risk factors (smoking, hypertension, diabetes, and hypercholesterolemia). They were compared with patients with at least one such risk factor after matching (3:1) on age, sex, and use of statins during the trials (N=492). Patients with modifiable risk factors had significantly higher systolic blood pressure, LDL-c, triglycerides, and hsCRP, at baseline. IVUS parameters at baseline were significantly better than in patients with modifiable risk factors. Percent atheroma volume, 35.7 ±8.6 vs. 38 ±8.8% (p=0.004) and total atheroma volume, 174.7 ± 80 vs. 190.9 ± 84 mm3 (p = 0.03) and vascular calcifications were fewer as well, 22.2 vs. 26.5% (p=0.025). The use of aspirin and statin before and during the trials was similar. The percentage of patients that showed progression of atherosclerosis was similar in both groups, 50.9% vs. 45.1% (p=0.20). This analysis showed that even without major, modifiable risk factors, patients did have atherosclerosis, albeit less when compared to those individuals with risk factors. Progression was observed in both groups with no significant difference in the rate of progression.


Does baseline LDL-c matters when using intensive LDL-c lowering interventions?

This brief report examined critical and clinically relevant questions; What is the impact of baseline LDL-c on observed benefit after intensive LDL-c lowering? Data of 53 RCTs (N=329 897) were evaluated in this meta-analysis. The relevant outcomes studies were cardiovascular mortality and major cardiovascular events (MACE). Patients were stratified according to baseline LDL-c levels. Similar to previous meta-analyses, each 1 mmol/l (38.9 mg/dl) lower LDL-c was associated with a 15% reduced cardiovascular mortality risk, RR: 0.85 (0.81-0.89); however, this varied by baseline levels of LDL-c (P=0.04 for interaction). Only patients with LDL-c >100 mg/dL showed a decrease cardiovascular mortality risk. The reduction in MACE was independent of baseline LDL-c. When comparing primary or secondary prevention patients, similar outcomes were observed. The authors concluded that current guideline recommendations to aim for >50% LDL-c reduction from baseline are valid and should be enforced in high CVD risk patients. Khan SU, Michos ED. Cardiovascular mortality after intensive LDL-Cholesterol lowering: Does baseline LDL-Cholesterol really matter? Am J Prev Cardiol 2020; 1:100013. http://www.ncbi.nlm.nih.gov/pubmed/?term=34327454
Comparing the US and European updated Lipid Management Guidelines

Recently both ACC/AHA and EAS/ESC have released new guidelines on lipid management, in 2018 and 2019, respectively. Both added important information from trials designed to reduce LDL-c to lower targets using novel, non-statin lipid-lowering drugs. Interpretation of the evidence is predominantly similar; however, differences might be confusing for those working in clinical practice that seek simple and straightforward answers. This article provides an in-depth comparison of the distinct differences of both guidelines, explains the rationale of these recommendations, and guides health care providers by answering three critical clinical questions: 1. Are ASCVD event rates similar in high-risk primary and stable secondary prevention? 2. Does imaging evidence of subclinical atherosclerosis justify aggressive use of statin and non-statin therapy (if needed) to reduce LDL-C levels below 55 mg/dL as recommended in the ESC/EAS Guideline? And 3. Do LDL-C levels below 70 mg/dL achieve a large ARR in secondary ASCVD prevention? In large the more cautious US approach, incorporating financial burden of novel treatments is the authors preferred choice where non-statins are recommended selectively for the high- and especially the very-high risk patients.


Relevant publications


2. Young RP, Scott RJ. Statins as adjunct therapy in COPD: is it time to target innate immunity and cardiovascular risk? The European respiratory journal 2021; 58.

3. Woo JS, Hong SJ, Cha DH et al. Comparison of the Efficacy and Safety of Atorvastatin 40 mg/ω-3 fatty acids 4 g Fixed-Dose Combination and Atorvastatin 40


Basic Science publications


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